

Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-29. (Cancelled)

30. (Previously presented) A method for synthesizing a templated molecule, comprising the steps of:

- a) providing at least one template comprising of one or more codons,
- b) providing a first functional entity attached to a first zipping oligonucleotide capable of reversible interaction with a second zipping oligonucleotide,
- c) providing one or more building blocks, each building block comprising a further functional entity linked to an anti-codon by a linker,

wherein the anti-codon complements a codon of the template,

wherein the further functional entity is connected to the second zipping oligonucleotide capable of reversible interaction with the first zipping oligonucleotide attached to the first functional entity provided in step b), and

wherein the further functional entity is capable of being chemically connected to the first functional entity provided in step b),

- d) contacting the components provided in steps a), b), and c) with each other under conditions allowing for
  - i) specific hybridization of building block

anti-codon(s) to the codon(s) of the template(s) and  
ii) dimerization of two zipping oligonucleotides  
attached to different functional entities,

- e) allowing a further functional entity of the one or more building blocks provided in step c) to form a chemical connection to the first functional entity provided in step b), and
- f) obtaining a templated molecule attached to the template which directed the synthesis thereof.

31. (Previously presented) The method of claim 30, wherein steps d) and e) are repeated one or more times prior to obtaining in step f) the templated molecule attached to the template which directed the synthesis thereof.

32. (Previously presented) The method of claim 30, wherein the first functional entity is covalently connected to the template.

33. (Previously presented) The method of claim 30, wherein the first functional entity is hybridized to the template.

34. (Previously presented) The method of claim 30, wherein the first functional entity forms part of a building block further comprising

an anti-codon complementing a template codon,

a linker connecting the anti-codon and the first functional entity, and

a first zipping oligonucleotide connected to the first functional entity.

35. (Previously presented) The method of claim 32,

wherein the first functional entity forms part of a building block further comprising

an anti-codon complementing a template codon,

a linker connecting the anti-codon and the first functional entity, and

a first zipping oligonucleotide connected to the first functional entity.

36. (Previously presented) The method of claim 33, wherein the first functional entity forms part of a building block further comprising

an anti-codon complementing a template codon,

a linker connecting the anti-codon and the first functional entity, and

a first zipping oligonucleotide connected to the first functional entity.

37. (Previously presented) The method of claim 30, wherein the zipping oligonucleotide of the first functional entity is present in the template.

38. (Previously presented) The method of claim 32, wherein the zipping oligonucleotide of the first functional entity is present in the template.

39. (Previously presented) The method of claim 34, wherein the zipping oligonucleotide of the first functional entity is present in the template.

40. (Previously presented) The method of claim 30, wherein the zipping oligonucleotides comprise complementary sequences of nucleic acids or nucleic acid analogs.

41. (Previously presented) The method of claim 32, wherein the zipping oligonucleotides comprise complementary sequences of nucleic acids or nucleic acid analogs.

42. (Previously presented) The method of claim 33, wherein the zipping oligonucleotides comprise complementary sequences of nucleic acids or nucleic acid analogs.

43. (Previously presented) The method of claim 30, wherein the first functional entity is further connected to a sequence of nucleic acids complementing a sequence of nucleic acids harbored by the template.

44. (Previously presented) The method of claim 32, wherein the first functional entity is further connected to a sequence of nucleic acids complementing a sequence of nucleic acids harbored by the template.

45. (Previously presented) The method of claim 33, wherein the first functional entity is further connected to a sequence of nucleic acids complementing a sequence of nucleic acids harbored by the template.

46. (Previously presented) The method of claim 30, wherein the zipping oligonucleotide forms part of the linker of the building block.

47. (Previously presented) The method of claim 34, wherein the zipping oligonucleotide forms part of the linker of the building block.

48. (Previously presented) The method of claim 37, wherein the zipping oligonucleotide is proximal to the functional entity.

49. (Previously presented) The method of claim 46, wherein the zipping oligonucleotide is proximal to the functional entity.

50. (Previously presented) The method of claim 46, wherein the zipping oligonucleotide is spaced from the first or further functional entity by no more than 2 nucleotides.

51. (Previously presented) The method of claim 48, wherein the zipping oligonucleotide is spaced from the first

or further functional entity by no more than 2 nucleotides.

52. (Previously presented) The method of claim 50, wherein the zipping oligonucleotide and the first functional entity is spaced by no more than 2 nucleotides.

53. (Previously presented) The method of claim 30, wherein the number of nucleotides which distance the first functional entity from the first zipping oligonucleotide is the same as the number of nucleotides which distance the further functional entity from the second zipping oligonucleotide.

54. (Previously presented) The method of claim 30, wherein the zipping oligonucleotides comprise from 3 to 20 nucleotides.

55. (Previously presented) The method of claim 54, wherein the zipping oligonucleotides comprise from 4 to 16 nucleotides.

56. (Previously presented) The method of claim 55, wherein the zipping oligonucleotides comprise from 5 to 10 nucleotides.

57. (Previously presented) The method of claim 30, wherein the linker in the building block between the anti-codon and the zipping oligonucleotide is a single bond.

58. (Previously presented) The method of claim 34, wherein the linker in the building block between the anti-codon and the zipping oligonucleotide is a single bond.

59. (Previously presented) The method of claim 30, wherein the hybridization of the building block anti-codon(s) to the template codons results in the formation of a codon:anti-codon hybrid, characterized by an annealing temperature, and the annealing temperature of the codon:anti-codon hybrid is higher than the annealing temperature of the hybridized zipping oligonucleotides.

60. (Previously presented) The method of claim 59, wherein the difference between the annealing temperatures is 10°C or more.

61. (Previously presented) The method of claim 59, wherein the difference between the annealing temperatures is 25°C or more.

62. (Previously presented) The method of claim 30, wherein the conditions for allowing specific hybridization of the building block anti-codon(s) to the codon(s) of the template(s) are distinct from the conditions allowing for optimal dimerisation of the two zipping oligonucleotides.

63. (Previously presented) The method of claim 62, wherein the conditions for allowing specific hybridization of the building block anti-codon(s) to the codon(s) of the template include a concentration of codons and/or anti-codons, which is higher than the concentration of codons and/or anti-codons used for dimerisation of the two zipping oligonucleotides.

64. (Previously presented) The method of claim 63, wherein the concentration during hybridization of codon(s) and anti-codons is at least 10 times higher than the concentration used for dimerisation of the two zipping oligonucleotides.

65. (Previously presented) The method of claim 30, wherein the contacting according to step d) is performed by alternating the temperature below and above the annealing temperature of the hybridized zipping oligonucleotides.

66. (Previously presented) The method of claim 65, wherein a plurality of temperature alternations are performed.

67. (Previously presented) The method of claim 65, wherein the highest temperature is below the annealing temperature of the codon:anti-codon hybrid.

68. (Previously presented) The method of claim 30, wherein the template codons have from 3 to 30 nucleotides.

69. (Previously presented) The method of claim 30, wherein at least two codons of the template are arranged in sequence next to each other and are separated by a spacer group.

70. (Previously presented) The method of claim 69,

wherein the template comprises further codons.

71. (Previously presented) The method of claim 70, wherein each further codon is separated by a spacer nucleotide sequence.

72. (Previously presented) The method of claim 69, wherein each spacer nucleotide sequence identifies the position of a corresponding codon.

73. (Previously presented) The method of claim 69, wherein the spacer nucleotide sequence contains a region of high affinity ensuring that the hybridization of the template with the anti-codon(s) occur in frame.

74. (Previously presented) The method of claim 69, wherein the spacer nucleotide sequence adjusts the codon:anti-codon annealing temperature.

75. (Previously presented) The method of claim 30, wherein the number of template codons is from 2 to 100.

76. (Previously presented) The method of claim 75, wherein the number of template codons is from 3 to 15.

77. (Previously presented) The method of claim 30, wherein the functional entity of the building block is a precursor of the functional entity which is incorporated into the templated molecule.

78. (Previously presented) The method of claim 77, wherein the structure of the functional entity is changed as a result of the incorporation of the functional entity into the templated molecule during its synthesis.

79. (Previously presented) The method of claim 30, wherein a functional entity of the one or more building blocks has from 1 to 10 reactive groups.

80. (Previously presented) The method of claim 79, wherein a building block featuring only one reactive group is used for generating end positions of polymers.

81. (Previously presented) The method of claim 79, wherein building blocks having two reactive groups are used for generating the body part of a polymer.

82. (Previously presented) The method of claim 79, wherein building blocks having two reactive groups are used for generating scaffolds capable of being reacted with further functional entities.

83. (Previously presented) The method of claim 82, wherein functional entities having two or more reactive groups are used for reactions with a scaffold in the form of a core structure comprising several reactive groups, wherein said reactions result in the formation of different templated molecules.

84. (Previously presented) The method of claim 82, wherein the reactions of the reactive groups are aided by fill-in groups or catalysts.

85. (Previously presented) The method of claim 30, wherein the anti-codon, the linker and the second zipping oligonucleotide of the one or more building block(s) forms a contiguous, linear oligonucleotide.

86. (Previously presented) The method of claim 30, wherein building block anti-codons are annealed to the template before the functional entities are connected to each other through a chemical reaction.

87. (Previously presented) The method of claim 30, wherein individual building blocks are added separately and contacted with the template.

88. (Previously presented) The method of claim 31, wherein building blocks contacting the template in a first reaction cycle result in the formation of codon:anti-codon hybrids with a lower annealing temperature than the annealing temperature of the codon:anti-codon hybrids which are formed when subsequently added, further building blocks are contacting the template in a second or further reaction cycle.

89. (Previously presented) The method of claim 88, wherein the annealing temperature of codon:anti-codon hybrids in the second or further reaction cycle results in maintaining only second or further round building blocks in contact with



the template, while the majority of the anti-codons of previous synthesis round building blocks, or anti-codons of non-reacted building blocks, become single stranded and are displaced from the template.

90. (Previously presented) The method of claim 31, wherein the anti-codon of a building block remain annealed to the template after the transfer of a building block functional entity to a scaffold and during a subsequent reaction cycle.

91. (Previously presented) The method of claim 31, wherein the anti-codon of a reacted building block is removed from the template prior to a repetition of steps d) and e).

92. (Previously presented) The method of claim 30 comprising the further step of transferring the templated molecule to an anchorage point on the template, or to a nucleotide sequence complementing the template, to establish a chemical connection between the template and the templated molecule which allows the even further steps of denaturing enrichment or denaturing post-templating modification of the templated molecule to be performed.

93. (Previously presented) The method of claim 92, wherein the chemical connection is a covalent chemical bond.

94. (Previously presented) The method of claim 92, wherein the hybrid formed between the complementing nucleotide sequence and the template has a higher annealing temperature than the annealing temperature of hybrid(s) formed between any of the building block anti-codons and the template.

95. (Previously presented) The method of claim 94, wherein stringency conditions are used during templated molecule enrichment which result in the clearance of used building blocks from the template.

96. (Previously presented) The method of claim 30, wherein the first functional entity is a scaffold which is reacted with two or more functional entities.

97. (Previously presented) The method of claim 96, wherein the scaffold is reacted with functional entities

emanating from building blocks.

98. (Previously presented) The method of claim 96, wherein the scaffold comprises two or more reactive groups.

99. (Previously presented) The method of claim 96, wherein the scaffold remains attached to the template through-out the synthesis of the templated molecule.

100. (Previously presented) The method of claim 30, wherein the scaffold forms part of a building block the anti-codon of which is annealed to a flanking position of the template, which flanking position is not located between the template codons.

101. (Previously presented) The method of claim 30, wherein the template comprises two or more codons, and wherein said building blocks attached to said two or more codons through their anti-codons have identical, complementary zipping oligonucleotides capable of dimerising in an ordered way.

102. (Previously presented) The method of claim 101, wherein the hybridization of codon(s) to anti-codon(s) and the dimerisation of zipping oligonucleotides occur in separate steps, wherein the conditions for specific hybridization of codon(s) to anti-codon(s) of the template(s) are distinct from the conditions for dimerisation of the zipping oligonucleotides.

103. (Previously presented) The method of claim 102, wherein the step of dimerisation of the zipping oligonucleotides is carried out under conditions ensuring that codons and anti-codons remain attached and under conditions allowing a reaction between functional entities on different building blocks.

104. (Previously presented) The method of claim 30, wherein the codon is a series of nucleotides in the form of nucleobases on a backbone, wherein said nucleobases are selected from the group consisting of natural nucleobases and non-natural nucleobases obeying Watson-Crick hydrogen bonding

rules.

105. (Currently amended) The method of ~~any of~~ claims 104, wherein the nucleobases are selected from the group consisting of adenine, guanine, thymine, cytosine, uracil, purine, xanthine, diaminopurine, 8-oxo-N<sup>6</sup>-methyladenine, 7-deazaxanthine, 7-deazaguanine, N<sup>4</sup>,N<sup>4</sup>-ethanocytosin, N<sup>6</sup>,N<sup>6</sup>-ethano-2,6-diamino-purine, 5-methylcytosine, 5-(C<sup>3</sup>-C<sup>6</sup>)-alkynylcytosine, 5-fluorouracil, 5-bromouracil, pseudoisocytosine, 2-hydroxy-5-methyl-4-triazolopyridine, isocytosine, isoguanine and inosine.

106. (Previously presented) The method of claim 104, wherein the backbone contains a sugar moiety and an internucleoside linker.

107. (Previously presented) The method of claim 106, wherein the backbone is a pentose selected from ribose, 2'-deoxyribose, 2'-O-methyl-ribose, 2'-flour-ribose and 2'-4'-O-methylene-ribose (LNA).

108. (Previously presented) The method of claim 107, wherein the nucleobase is attached to the 1' position of the pentose.

109. (Previously presented) The method of claim 107, wherein the internucleoside linker connects the 3' end of a preceding monomer to a 5' end of a succeeding monomer when the sugar moiety of the backbone is a pentose.

110. (Previously presented) The method of claim 109, wherein the internucleoside linker is a phosphodiester bond.

111. (Previously presented) The method of claim 109, wherein the internucleoside linker is a bond selected from phosphorothioate bonds, methylphosphonate bonds, phosphoramidate bonds, phosphotriester bonds and phosphodithioate bonds.

112. (Previously presented) The method of claim 30, wherein the template is immobilised on a solid support.

113. (Previously presented) The method of claim 112, wherein the solid support is a bead.

114. (Previously presented) The method of claim 112, wherein a biotin group is incorporated in the template, and wherein the solid support is as matrix material coated with streptavidin.

115. (Previously presented) The method of claim 30, wherein the first functional entity is linked to the template through a selectively cleavable linker which enables the separation of the synthesized, template-directed molecule from the template at a predetermined time.

116. (Previously presented) The method of claim 115, wherein the first functional entity is a scaffold.

117. (Previously presented) A method for generating a library of different bifunctional complexes, said method comprising the steps of subjecting a plurality of templates to the method according to claim 30, thereby generating a library of different bifunctional complexes each comprising a templated molecule attached to the template or complementary template which directed the synthesis of the templated molecule.

118. (Previously presented) The method of claim 117, wherein the number of different bifunctional complexes in the library is at least  $10^3$ .

119. (Previously presented) The method of claim 117, wherein the number of different bifunctional complexes in the library is at least  $10^6$ .

120. (Previously presented) The method of claim 117, wherein the number of different bifunctional complexes in the library is at least  $10^9$ .

121. (Previously presented) The method of claim 117, wherein a plurality of different templates is provided in step a) of claim 1 and wherein a plurality of different building blocks is provided in step c) of claim 1.

122. (Previously presented) A method for generating a library of different bifunctional complexes, said method comprising the steps of subjecting a plurality of templates

simultaneously to the method according to claim 30, thereby generating a library of different bifunctional complexes each comprising a templated molecule attached to the template or complementary template which directed the synthesis of the templated molecule.

123. (Previously presented) The method of claim 117, wherein the templated molecules of the library are synthesized by sequentially contacting the templates with subsets of building blocks to be used in the synthesis of the templated molecules.

124. (Previously presented) The method of claim 117, wherein each template comprises a number of coding sections, and wherein each coding section specifies one or more unique codons.

125. (Previously presented) The method of claim 124, wherein the coding sections are positioned in a linear sequence with individual coding sections positioned immediately next to each other.

126. (Previously presented) The method of claim 125, wherein the coding sections are interspaced by a spacer sequence.

127. (Previously presented) The method of claim 124, wherein the template is branched.

128. (Previously presented) The method of claim 124, wherein each template has from 2 to 50 coding regions.

129. (Previously presented) The method of claim 124, wherein each template has from 3 to 30 coding regions.

130. (Previously presented) The method of claim 124, wherein each template has from 4 to 15 coding regions.

131. (Previously presented) The method of claim 128, wherein the number of unique codons in each coding region is the same.

132. (Previously presented) The method of claim 128, wherein each coding region contains a different number of unique codons.

133. (Previously presented) The method of claim 128, wherein each coding region contains a single unique codon.

134. (Previously presented) The method of claim 117 comprising the further step of subjecting the library of bifunctional complexes to an enrichment comprising the steps of

- i) exposing the library to conditions enriching the library with complexes having a predetermined activity,
- ii) amplifying the complexes of the enriched library,
- iii) obtaining an enriched library having a higher ratio of complexes comprising templated molecules with the predetermined activity.

135. (Previously presented) The method of claim 134, wherein the amplification of the complexes of the enriched library comprises the steps of contacting the library of complexes with amplification means, amplifying the templates or the complementing templates, and conducting the method of any of claims 1 to 75 using the amplification product(s) as templates.

136. (Previously presented) The method of claim 134, wherein steps i) and ii) are repeated from 2 to 5 times.

137. (Previously presented) The method of claim 136, wherein generated complexes are identified after the completion of each cycle of repetition.

138. (Previously presented) The method of claim 136, wherein the complexes are identified after the last repetition cycle.

139. (Previously presented) The method of claim 137, wherein the identification after the enrichment involves determination of the sequence of the template and/or structural determination of the templated molecule and/or the entire complex having the predetermined activity.

140. (Previously presented) The method of 134, wherein

enrichment of library complexes is obtained by screening for complexes having an affinity for or an effect on a target molecule.

141. (Previously presented) The method of claim 140, wherein the target molecule is selected from soluble receptors, cell surface receptors, enzyme inhibitors and surface epitopes.

142. (Previously presented) The method of claim 140, wherein the target molecule is selected from receptors, enzymes, hormones, transcription factors, ion channels and DNA.

143. (Previously presented) The method of claim 142, wherein the target molecule is selected from receptors and enzymes.

144. (Previously presented) The method of claim 143, wherein the target molecule is selected from G protein coupled receptors and proteases.

145. (Previously presented) The method of claim 30, comprising the further step of contacting the templated molecule with a target molecule selected from receptors, enzymes, hormones, transcription factors, ion channels and DNA, and identifying a templated molecule contacting a target molecule as an agonist or an antagonist for the target molecule.

146. (Currently amended) A bifunctional complex comprising a templated molecule attached to the template which directed the synthesis thereof, wherein said template is further attached to at least two zipping oligonucleotides capable of reversibly dimerizing in an ordered way, said bifunctional complex being obtainable by the method of claim 30, wherein at least one of the following conditions applies:

- (i) the templated molecule is a beta-peptide,
- (ii) the templated molecule is a gamma-peptide,
- (iii) the templated molecule is an omega-peptide,
- (iv) the templated molecule is a cyclohexane- and

cyclopentane-backbone modified beta-peptide,

(v) the templated molecule is a vinylogous polypeptide,

(vi) the templated molecule is a peptide having  
prosthetic group(s),

(vii) the templated molecule is an aliphatic polycycle,

(viii) the templated molecule is an aromatic polycycle,

(ix) the templated molecule is a polyheterocycle,

(x) the templated molecule is a monofunctional,  
difunctional or trifunctional, nonaromatic carbocycle,

(xi) the templated molecule is a monocyclic, bicyclic or  
tricyclic hydrocarbon,

(xii) the templated molecule is a monofunctional,  
difunctional or trifunctional nonaromatic heterocycle,

(xiii) the templated molecule is a monocyclic, bicyclic  
or tricyclic heterocycles,

(xiv) the templated molecule is a bridged polycyclic  
heterocycle,

(xv) the templated molecule is a monofunctional,  
difunctional or trifunctional aromatic carbocycle,

(xvi) the templated molecule is a monocyclic, bicyclic  
or tricyclic aromatic carbocycle,

(xvii) the templated molecule is a monofunctional,  
difunctional or trifunctional aromatic heterocycle,

(xviii) the templated molecule is a monocyclic, bicyclic  
or tricyclic heterocycle, or

(xix) the templated molecule is a steroid.

147. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a beta-peptide.

148. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a gamma-peptide.

149. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is an



omega-peptide.

150. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a cyclohexane- and cyclopentane-backbone modified beta-peptide.

151. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a vinylogous polypeptide.

152. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a peptide having prosthetic group(s).

153. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is an aliphatic polycycle.

154. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is an aromatic polycycle.

155. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a polyheterocycle.

156. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monofunctional, difunctional or trifunctional, nonaromatic carbocycle.

157. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monocyclic, bicyclic or tricyclic hydrocarbon.

158. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monofunctional, difunctional or trifunctional nonaromatic heterocycle.

159. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monocyclic, bicyclic or tricyclic heterocycles.

160. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a

bridged polycyclic heterocycle.

161. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monofunctional, difunctional or trifunctional aromatic carbocycle.

162. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monocyclic, bicyclic or tricyclic aromatic carbocycle.

163. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monofunctional, difunctional or trifunctional aromatic heterocycle.

164. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a monocyclic, bicyclic or tricyclic heterocycle.

165. (Previously presented) The bifunctional complex according to claim 146, wherein the templated molecule is a steroid.

166. (Previously presented) A library of different bifunctional complexes according to claim 146.

167. (Previously presented) The library according to claim 166, wherein each bifunctional complex comprises a different templated molecule.

168. (Previously presented) The library according to claim 166, wherein the number of different bifunctional complexes in the library is at least  $10^3$ .

169. (Previously presented) The library according to claim 166, wherein the number of different bifunctional complexes in the library is at least  $10^6$ .

170. (Previously presented) The library according to claim 166, wherein the number of different bifunctional complexes in the library is at least  $10^9$ .